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Efficacy, Safety and Mechanisms of Acupuncture and Electroacupuncture for Pain: A Narrative Review

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ABSTRACT

Research into the efficacy and safety of acupuncture and electroacupuncture for the relief of various types of pain, as well as the underpinning physiological mechanisms, has been ongoing since the 1950s. Recent trends have shown a significant increase in both the quantity and quality of studies, with an increasing range of pain types being supported by high and moderate certainty evidence. The primary aim of this narrative review is to provide an overview of the most robust evidence currently available to support the efficacy of acupuncture for inflammatory, neuropathic, and visceral pain, as well as pain in different clinical contexts. This evidence synthesis brings together the results of systematic reviews, meta-analyses, umbrella or overview reviews, and evidence maps. The secondary aim of this review is to explore animal and human studies on the mechanisms of acupuncture and electroacupuncture in pain relief. Despite potential underestimation of effect sizes in existing studies, high to moderate certainty evidence supports the efficacy of acupuncture and electroacupuncture in managing a broad range of acute and chronic pain conditions, with a consistently favourable safety profile. These interventions have been shown to induce lasting neuromodulatory effects in both central and peripheral nervous systems, partly through the reversal of maladaptive neuroplasticity and sustained modulation of central and peripheral nervous system activity. Emerging evidence highlights the analgesic, antihyperalgesic, and anti-inflammatory properties of acupuncture and electroacupuncture, underscoring their potential in contemporary pain management.

Introduction

Early research into acupuncture's effectiveness for pain relief was initially based in Asian countries with a longstanding tradition of acupuncture practice such as China, Korea, and Japan. Over more recent decades research efforts have spread globally. The quality of acupuncture research has improved significantly, largely due to the development of guidelines for the conduct and reporting of acupuncture research such as CONSORT, STRICTA, and NICMAN, and the establishment of organisations such as the Society for Acupuncture Research. The number of clinical trials of acupuncture listed in the Cochrane Database of Clinical Trials has grown from 2,015 in February 2009 to 21,499 in June 2025.

Acupuncture has been recommended in an increasing number of clinical practice guidelines around the world as either an adjunctive or stand-alone intervention.[1]

The physiological mechanisms underpinning acupuncture were poorly understood at first, but have advanced rapidly due to major discoveries such as the Melzack and Wall Pain Control Gate theory which elucidated the role of the dorsal horn of the spine, and also the discovery of endogenous opioids such as enkephalins, endorphins, dynorphins, and endomorphins.[2,3] The seminal work of Han et al[4] from Beijing clarified the ascending and descending pathways of the acupuncture signal, as well as identified the so-called "mesolimbic neuronal loop of analgesia" in the brain stem and brain. More recently, the importance of numerous other mediators in acupuncture's analgesic effects such as adenosine, serotonin, norepinephrine, dopamine, somatostatin, glutamate, and cholecystokinin octapeptide (CCK8), as well as receptors such as transient receptor potential vanilloid 1 (TRPV1) and N-methyl-D-aspartate (NMDA) receptors, is becoming clearer. Signalling pathways mediating both the analgesic and anti-inflammatory effects of acupuncture have also been, and continue to be, characterised.

Overviews and evidence maps of acupuncture for chronic pain

Several overview reviews and evidence maps of the effectiveness of acupuncture have been published since 2012, with the most recent published in February 2025.[5-12] Three different grading systems were used – evidence of positive effect/evidence of potential positive effect/unclear evidence/no evidence of effect; high/moderate/low/very low certainty of evidence; effective (superior to sham acupuncture or no acupuncture control and clinically significant effects). The effectiveness of acupuncture for the relief of chronic pain was strongly supported, especially non-specific myofascial/ musculoskeletal pain such as low back pain, shoulder pain, neck pain and knee osteoarthritis (see Table 1). Acupuncture for migraine prophylaxis and tension-type headache was also supported by robust evidence, and acupuncture is recommended for both conditions in the National Institute for Health and Care Excellence (NICE) clinical practice guidelines in the United Kingdom (UK).[13] Fibromyalgia pain was also rated highly in the four most recent reviews.[9-12]

A notable feature of acupuncture for chronic pain highlighted by Vickers et al in their 2012 individual patient data meta-analyses (MA) from 17,922 patients, and 2017 update including 20,827 patients, was the sustained analgesic effect still evident at 12 months after treatment ceased.[5,8] In the 2012 paper, patients reported 90% of the pain relief at 12 months as they experienced immediately after the last treatment, while in the 2017 paper the figure was 85%.[5,8]

Acupuncture for chronic and acute myofascial pain

ACUPUNCTURE FOR LOW BACK PAIN

More research has been conducted on acupuncture for low back pain than for any other pain-related condition. Most of these studies have focused on chronic non-specific low back (CNSLBP), while only a few studies have addressed acute low back pain. Controversy has surrounded placebo/sham controlled randomised trials (RCTs) and how to interpret them for two main reasons worth exploring in more detail. The first issue is that while acupuncture and electroacupuncture (EA) have consistently shown clinical benefits, the differences between the verum and sham groups in RCTs have often been relatively small.[5] When interpreting this research, if emphasis is placed on effectiveness, then acupuncture is consistently recommended for CNSLBP. However, if efficacy (the difference in effect size between verum and sham acupuncture) is prioritised, then acupuncture for CNSLBP is sometimes not recommended. This disparity has been referred to as "The Efficacy Paradox" leading to more effective treatments being rejected in favour of less effective treatments which show greater efficacy. This can be illustrated by the decision-making on acupuncture for CNSLBP by NICE in the UK. Acupuncture was recommended by NICE in 2009, but in 2016 this was dramatically reversed to recommended against its use.[14] Shortly after this decision, the American College of Physicians updated their guidelines to give a strong recommendation for acupuncture for CNSLBP with moderate evidence, and similarly, a strong recommendation for acupuncture for acute low back pain with low evidence[15]. The second issue, which is a problem for all placebo/sham controlled acupuncture research, and more broadly for all placebo/sham controls for complex interventions, is establishing that a sham protocol is both inert and indistinguishable to the subject.[16-18] Problems with either sham protocols not being inert or verum protocols being suboptimal may lead to an underestimation of the effect size of acupuncture and introduce negative bias into systematic reviews (SRs), MAs, and clinical practice guidelines.[17,18]

ACUPUNCTURE FOR SHOULDER PAIN

Shoulder pain was the only pain condition supported by high certainty evidence in both the evidence maps from the British Medical Journal (BMJ) and the US Veterans Affairs Department (USVA)(2022).[10,11] Subsequent SRs and MAs have found that acupuncture alone, or combined with physiotherapy, improved pain in the short to medium term (up to 3 months), and reduced disability.[19,20]

ACUPUNCTURE FOR NECK PAIN

The BMJ evidence map found high certainty evidence for

acupuncture for the short term relief of neck pain.[10] A SR and MA published since found that acupuncture may relieve chronic neck pain for up to 3 months and improved functional impairment for more than 3 months.[21] A SR and MA on acupuncture for whiplash found moderate certainty evidence for pain relief.[22] In another SR and MA, Zhao et al[23] concluded that acupuncture is superior to traction therapy for pain relief in radicular cervical spondylosis.

ACUPUNCTURE FOR OSTEOARTHRITIS PAIN

Acupuncture research on osteoarthritis and how findings should be interpreted is another area of controversy.[14,24] Some researchers have suggested that the effect size of acupuncture may have been underestimated in some osteoarthritis studies due to either selection of non-inert acupuncture points in the sham control arm or due to inadequate frequency and duration of the verum treatment regime.[25,26] A MA by Luo et al[27] found that EA was more effective for pain relief in knee osteoarthritis than manual acupuncture and suggested that stronger electrical stimulation may produce better outcomes than weak stimulation. Zhu et al[28] reported that acupuncture plus moxibustion produced superior improvement in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores for pain, stiffness, and physical function, along with fewer adverse events than other forms of standard care.

ACUPUNCTURE FOR FIBROMYALGIA

A SR by Patel et al[9] in 2020 on acupuncture for five types of chronic pain rated fibromyalgia pain as one of the two types of pain for which acupuncture was the most effective. Acupuncture for fibromyalgia pain was supported by high certainty evidence in the USVA evidence map and by moderate certainty evidence in the BMJ evidence map.[10,11] The State of Evidence review published in February 2025 rated the evidence supporting acupuncture for fibromyalgia pain as potential positive effect.[12]

ACUPUNCTURE FOR HEADACHE

Acupuncture for migraine prophylaxis has been found to be effective in seven of the eight reviews/evidence maps included in this review (see Table 1). NICE clinical practice guidelines have recommended acupuncture for migraine prophylaxis since 2009 and continue to do so.[13] Acupuncture for tension-type headache is similarly recommended in NICE guidelines and has been consistently rated as evidence of positive effect (see Table 1).

Table 1. Conditions with high or moderate certainty evidence/evidence of positive or potential positive effect according to overviews and evidence maps of acupuncture (2012-2025)

Condition	**Vickers et al 2012[1]**	**USVA Evidence Map 2014[2]**	**Acupuncture Evidence Project 2017[3]**	**Vickers et al 2017[4]**	**Patel et al 2020[5]**	**BMJ Evidence Map 2022[6]**	**USVA Evidence Map 2022[7]**	**State of evidence in acupuncture 2025[8]**
Chronic pain	Effective*	**Positive**		Effective*	Effective*		Moderate	**Positive**
Immediate pain relief							Moderate	Potential positive
Non-specific myofascial pain				Effective*		Moderate	Moderate	Potential positive
Low back pain	Effective*		**Positive**	Effective*	Effective*	Moderate		**Positive**
Shoulder pain	Effective*		Potential positive	Effective*		**High**	**High**	
Neck pain	Effective*		Potential positive	Effective*	Effective short term*	**High**		
Osteoarthritis	Effective*	Potential positive		Effective*				
Knee osteoarthritis	Effective*		**Positive**					**Positive**
Migraine prophylaxis	Effective*	**Positive**	**Positive**	Effective*	Most effective*		Moderate	**Positive**
Tension type headache	Effective*	**Positive**	**Positive**	Effective*			Moderate	**Positive**
Chronic headache	Effective*			Effective*				
CP/CPPS		Potential positive	Potential positive				Moderate	**Positive**
Fibromyalgia					Most effective*	Moderate	**High**	Potential positive
Peri-/post operative pain			**Positive**				Moderate	Potential positive
Post-herpetic neuralgia							Moderate	Potential positive

Condition	Vickers et al 2012[1]	USVA Evidence Map 2014[2]	Acupuncture Evidence Project 2017[3]	Vickers et al 2017[4]	Patel et al 2020[5]	BMJ Evidence Map 2022[6]	USVA Evidence Map 2022[7]	State of evidence in acupuncture 2025[8]
TMD		Potential positive					Moderate	
Diabetic peripheral neuropathy								Potential positive
CIPN								Potential positive
Sciatica			Potential positive					Potential positive
Lateral epicondylitis			Potential positive					Potential positive
ME/CFS								Potential positive
Cancer-related pain		Potential positive						Potential positive
IBS-D			Potential positive					Potential positive
Rheumatoid arthritis								Potential positive
Abdominal pain					Least effective*			
Plantar fasciitis		Potential positive	Potential positive					
Post-stroke shoulder pain			Potential positive					
Endometriosis								Potential positive
Dysmenorrhoea		Potential positive						Potential positive
Labour pain		Potential positive	Potential positive					Potential positive
PCOS								Potential positive
PMS								Potential positive
Back pain in pregnancy		Potential positive	Potential positive					

Abbreviations: CP/CPPS – chronic prostatitis/chronic pelvic pain syndrome, TMD – temporomandibular disorder, CIPN – chemotherapy-induced peripheral neuropathy, ME/CFS – myalgic encephalitis/chronic fatigue syndrome, IBS-D – irritable bowel syndrome – diarrhoea predominant, PCOS – polycystic ovarian syndrome, PMS – premenstrual syndrome
*Effective – superior to sham acupuncture and clinically significant effect

ACUPUNCTURE FOR CANCER-RELATED PAIN

The inclusion of acupuncture in cancer care has become known as a part of integrative oncology. A recent clinical practice guideline on integrative oncology for cancer pain has been developed by the Society for Integrative Oncology and the American Society of Clinical Oncology.[29] This guideline recommends acupuncture for adults with aromatase inhibitor-related joint pain, general cancer pain or musculoskeletal pain. However, no recommendations are made for paediatrics due to a lack of evidence. Acupuncture for cancer-related pain was rated as evidence of potential positive effect in two reviews.[6,12]

ACUPUNCTURE FOR PAIN IN GYNAECOLOGY AND OBSTETRICS

Acupuncture or acupressure for labour pain was rated as evidence of potential positive effect in three reviews.[6,7,11] A SR and MA by Giese et al[30] found that acupuncture produces clinically relevant relief of pelvic pain associated with endometriosis with low rates of adverse events. A SR and MA by Chen et al[31] found that acupuncture improves pain associated with endometriosis by modulating abnormal levels of prostaglandins, beta-endorphin, dynorphins, electrolytes, and substance P (SP). The State of Evidence review rated acupuncture for endometriosis pain as evidence of potential positive effect.[12]

Acupuncture was also rated as evidence of potential positive effect for the following types of pain in women's health: dysmenorrhoea,[6,12] polycystic ovary syndrome,[12] premenstrual syndrome,[12] and back pain in pregnancy.[6,7]

ACUPUNCTURE FOR PAEDIATRIC PAIN

Research on acupuncture and acupressure for pain in paediatrics is currently quite limited and despite some positive outcomes being reported, the evidence is currently weak.[32-36]

ACUPUNCTURE FOR CHRONIC PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME (CP/CPPS)

Acupuncture for CP/CPPS was rated as evidence of potential positive effect in the USVA evidence map (2014) and the Acupuncture Evidence Project (2016), moderate certainty evidence in the USVA evidence map (2022), and evidence of positive effect in the State of Evidence review (2025).[6,7,11,12] A SR and MA by Pan et al[37], which included 10 high quality RCTs (798 patients), found that acupuncture was superior to both sham acupuncture and standard care in pain score, National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) score, quality of life, urinary symptoms, and efficacy rate.

ACUPUNCTURE FOR PERI-OPERATIVE/POST-OPERATIVE PAIN

Acupuncture for the relief of peri-operative/post-operative pain was rated as evidence of positive effect in the Acupuncture Evidence Project, moderate certainty evidence in USVA evidence map (2022) and evidence of potential positive effect in the State of Evidence review.[7,11,12] Acupuncture has been shown to reduce pain and improve function following total knee arthroplasty with low adverse events and may even contribute to preventing commonly occurring post-surgical adverse events.[38-40]

ACUPUNCTURE FOR ACUTE PAIN IN EMERGENCY DEPARTMENT

In 2022, the Academic Consortium Pain Task Force published a White Paper Update reviewing acupuncture evidence for the management of acute pain in acute pain settings in hospitals including surgery, Intensive Care Unit, and Emergency Department..[41] The White Paper highlighted the potential for acupuncture treatment to reduce opioid use in acute pain management with a very low risk profile. An RCT comparing intravenous (IV) morphine with acupuncture in an Emergency Department to manage acute pain found that acupuncture produced satisfactory pain relief faster than IV morphine, with a higher responder rate (92% vs 78%), and fewer adverse events (56.6% vs 2.6%).[42]

ACUPUNCTURE FOR PAIN IN CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY (CIPN)

A recent umbrella review of 14 SRs found that both manual acupuncture and EA effectively alleviated CIPN symptoms, reduced CIPN pain, improved both motor and sensory nerve conduction velocity, and enhanced quality of life.[43] The State of Evidence review rated acupuncture for CIPN pain as evidence of potential positive effect.[12]

ACUPUNCTURE FOR PAIN IN DIABETIC PERIPHERAL NEUROPATHY (DPN)

The State of Evidence review rated acupuncture for DPN pain as evidence of potential positive effect.[12] In a SR and MA of 36 studies of DPN (2,739 patients) acupuncture improved pain intensity, motor and sensory nerve conduction velocities, depression score, Toronto clinical scoring system (TCSS) score, and quality of life.[44]

ACUPUNCTURE FOR POST-HERPETIC NEURALGIA

Acupuncture for post-herpetic neuralgia was rated as moderate certainty evidence in the USVA evidence map (2022) and evidence of potential positive effect in the State of Evidence review.[11,12] A SR and MA by Pei et al[45] found that acupuncture may reduce pain intensity, relieve anxiety and improve quality of life in patients with post-herpetic neuralgia.

Mechanisms

Research into the mechanisms by which acupuncture and EA reduce pain was initially focused on identifying neural pathways – ascending pathways, the brain and brain stem centres involved (the mesolimbic neuronal loop of analgesia), and the descending inhibitory pathways. With the discovery of endogenous opioid mediators, research began to concentrate more on opioid and non-opioid mediators and their receptors. More recently, signalling pathways have been identified and imaging technologies such as functional magnetic resonance imaging (fMRI) have opened up new opportunities to study the complex interactions between centres in the brain and brain stem in real-time response to acupuncture and EA in human subjects.

The seminal work of Han et al[46] used microinjections of specific opioid antagonists into various brain and brain stem centres, and spinal cord in animal models to observe what blocked the analgesic effects of EA. This research ultimately established the specificity of electrical frequencies of EA to elicit different opioid mediators – low frequency (2Hz) to produce enkephalins, beta-endorphin and endomorphins, and high frequency (100Hz) to generate dynorphins. In the spinal cord of rats, endomorphins activate mu opioid receptors (MOR), dynorphins activate kappa opioid receptors (KOR) while enkephalins and beta-endorphin activate both MOR and delta opioid receptors (DOR).[47]

BRAIN AND BRAIN STEM CENTRES IN ACUPUNCTURE ANALGESIA

The mesolimbic neuronal loop of analgesia was initially identified between periaqueductal gray (PAG) and nucleus accumbens, and was found to be mediated by serotonin and enkephalin.[4] Subsequent human studies using fMRI have identified several additional neural centres involved in acupuncture analgesia.

A review by Zhao et al[48] identified the following centres involved in acupuncture analgesia: nucleus raphe magnus (NRM), PAG, locus coeruleus, arcuate nucleus, preoptic area, nucleus submedius, lateral habenula (LHb), nucleus accumbens, caudate nucleus, septal area, and amygdala.

He et al[49] noted that, in fMRI studies of acupuncture analgesia, distinct patterns of brain region activations and deactivations were seen in different pain types and when different stimulation modes were used. The primary regions activated were the frontal, parietal, and temporal lobes, with key areas including the anterior cingulate cortex (ACC), insula, prefrontal cortex (PFC), and primary somatosensory cortex (S1).[49]

MEDIATORS AND RECEPTORS

Opioid mediators which participate in acupuncture analgesia include enkephalins, beta-endorphin, dynorphins, endomorphins, and nociception/orphaninFQ.[48] Non-opioid mediators, some of which interact with opioid mediators, include SP, adenosine, serotonin, dopamine, norepinephrine/noradrenalin, acetylcholine, glutamate, gamma amino butyric acid (GABA), somatostatin, neurotensin, nitric oxide, anandamide, and CCK8.[48,50] Neurotrophins, notably brain-derived neurotrophic factor (BDNF), have also been suggested to play a role in regulating neural plasticity in neuropathic pain.[51]

Signalling pathways

A review by Zhao et al[48] identified the PTX-sensitive Gi/o protein- and MAP kinase-mediated signalling pathways as well as the downstream events NF-kappaB, c-fos and c-jun as participants in EA analgesia. Signalling pathways in inflammatory pain and neuropathic pain are detailed in the following sections.

INFLAMMATORY PAIN

In a review on the peripheral receptors and mediators involved in the antihyperalgesic effects of acupuncture, Trento et al[50] identified the following receptor families and mediator types: opioid, adenosine, cannabinoid, TRPV, histamine, adrenergic, muscarinic, corticotrophin releasing factor, interleukin-1, and endothelin receptors; opioid peptides, adenosine, histamine, SP, calcitonin gene-related peptide (CGRP), anandamide, nitric oxide, and norepinephrine. Trento et al also note that in the local region of acupuncture points adenosine, histamine, TRPV, and adrenergic receptors play key roles in the signalling of acupuncture needling.[50] Another review of the anti-inflammatory and antihyperalgesic effects of acupuncture proposed that there may be complex crosstalk between proinflammatory neuropeptides, cytokines, chemokines, and neurotrophins, and between adenosine, chemokine, opioid, neurotrophin, dopamine, cannabinoid, and TRPV1 receptors.[52] The same review identified the following signalling pathways involved in acupuncture's effects in reducing allodynia and/or thermal hyperalgesia: TrkA/PI3K/PIP3/Akt, PLA2/LO, PLCb/PKC, p38 MAPK/ATF-2/TRPV1, ASIC3, Nav1.7, Nav1.8, ERK1/2-COX-2, ERK1/2-CREB-NK-1, JNK1/2, p35/p25/Cdk5/MAPK, p35/p25/Cdk5/NMDA.[52]

The role of purinergic signalling in the acupuncture treatment of inflammatory pain was first established by Goldman et al[53] in 2010. More recent studies have shown that acupuncture increases adenosine triphosphate dephosphorylation thereby decreasing the signalling activity of downstream P2X3, P2X4, and P2X7 receptors, and regulates levels of pro-inflammatory cytokines, neurotrophins, and synapsin1.[54,55] Acupuncture also promotes the production of adenosine, enhancing the expression of adenosine A1 and A2A receptors.[54]

Zhang et al[56] described the peripheral and central mechanisms of acupuncture for inflammatory pain. Peripheral mechanisms are reported to involve immune cells and neurons, purinergic signalling, nociceptive ion channels, cannabinoid receptors, and endogenous opioids.[56] Central nervous system mechanisms involve TPRV1, glutamate (and glutamate receptors), glial cells, GABAergic interneurons, and signalling molecules.[56]

NEUROPATHIC PAIN

A review of animal research by Su et al[57] reported that the brain nuclei involved in the relief of neuropathic pain by acupuncture included the PAG, LHb, mPFC, and ACC, while the related brain circuits included the PAG-LHb and mPFC-ACC. Acupuncture was also found to improve synaptic plasticity.[57] The acupuncture-induced release of glutamate, GABA, serotonin, and other neurotransmitters and receptors in the brain tissues assisted in maintaining the balance between excitatory and inhibitory neurons.[57] Acupuncture also reduced brain inflammation by down-regulating the release of pro-inflammatory cytokines such as interleukins and inhibited the overactivation of glial cells.[57] Finally, acupuncture also assisted in maintaining homeostasis of glucose metabolism.[57]

A review by Jang et al[58] on chronic neuropathic pain suggests that acupuncture may modulate DNA methylation within the central nervous system. Specifically, acupuncture may adjust the DNA methylation of genes related to mitochondrial dysfunction, oxidative phosphorylation, and inflammatory pathways within the PFC, ACC, and S1.[58] Furthermore, Jang et al suggests that acupuncture may influence DNA methylation of genes associated with neurogenesis in hippocampal neurons.[58]

In a review on acupuncture for radicular pain, Li et al[59] postulates several mechanisms by which acupuncture relieves pain. Acupuncture reduces muscle spasms which may be impinging nerve roots, improves peripheral microcirculation, reduces release of pro-inflammatory cytokines via inhibition of the HMGB1/RAGE and TLR4/NF-κB signalling pathways, influences synaptic plasticity within the spinal cord, and modulates brain function within the default mode network, notably the mPFC, ACC, and thalamus.

VISCERAL PAIN

A review on acupuncture for visceral pain by Dou et al[60] found modulation of the following centres: nucleus tractus solitarius, parabrachial nucleus, ACC, rostral ventromedial medulla (RVM), locus coeruleus, and amygdala.[60] Acupuncture is reported to influence functional connections between different brain regions, these neural circuits including PBN-amygdala, locus coeruleus-RVM, amygdala-insula, ACC-amygdala, claustrum-ACC, bed nucleus of the stria terminalis-paraventricular nucleus (PVN), and the PVN-ventral lateral septum circuit. [60] Dou et al also suggest that regulating glucose metabolism may also play a role in acupuncture's effects on visceral pain.[60]

In acupuncture for visceral pain, Lee et al[61] reported changes in the concentrations of beta-endorphin, epinephrine, cortisol, and prostaglandin E2 in plasma, the levels of c-Fos, SP, corticotropin-releasing hormone, P2X3, acetylcholinesterase, NMDA receptors, and serotonin in the gut/spinal cord, and the neuronal activity of the thalamus.

NEUROPLASTICITY

A landmark study by Napadow et al[62] demonstrated the ability of EA to reverse adverse neuroplastic changes in the somatosensory cortex in a patient with carpal tunnel syndrome pain. Synaptic neuroplasticity has been cited as one of the potential mechanisms of acupuncture analgesia in neuropathic pain and involvement of BDNF has also been suggested.[51,57,59] Neuromodulation of central and peripheral nervous systems is also suggested by the longevity of acupuncture analgesic effects with persistence of 85% to 90% of pain relief 12 months after treatment.[5,8] Improvements in motor and sensory nerve conduction velocities reported in patients with CIPN and DPN further suggest neurogenesis of peripheral nerves with the action of neurotrophins and improved microcirculation being offered as possible explanations.[63]

GLYMPHATIC SYSTEM

The glymphatic system clears metabolic waste, such as amyloid beta and lactate from the parenchyma during sleep via perivascular spaces.[64] The glymphatic system is regulated by sleep and norepinephrine which inhibits fluid movement during wakefulness.[64] Norepinephrine is also essential in the process whereby acute pain becomes chronic.[64] Chronic neuropathic pain is frequently associated with disrupted sleep.[64] Acupuncture can relieve chronic neuropathic pain by reducing norepinephrine and increasing glymphatic function.[64] Furthermore, acupuncture has also been reported to be effective for the treatment of insomnia.[65]

ADVERSE EVENTS

Serious adverse events due to acupuncture and EA have been reported to be rare, while some minor adverse events such as minor bruising, pain and vasovagal responses are more common. [66,67] Appropriate training of acupuncture practitioners can mitigate the risk of adverse events.[66,67]

Discussion

It has long been established that acupuncture analgesia is not effective for all individuals, and this phenomenon of "non-responders" was initially attributed to the antagonistic action of CCK8.[48]. Zhao et al[48] also suggests that perhaps angiotensin II may play a similar antagonistic role to acupuncture analgesia. Some early research also suggests that differences in response to acupuncture analgesia may have some genetic basis.[48]

The body of research literature supporting the effectiveness of acupuncture and EA for pain relief is now substantial and includes many SRs and MAs. However, when interpreting the clinical relevance of acupuncture as a treatment option for specific types of pain, clinical practice guideline development has been beset with controversy, notably around CNSLBP and osteoarthritis. In placebo/sham controlled RCTs, while effectiveness of acupuncture for pain has been consistently demonstrated, sometimes small differences between verum and sham arms has led to small estimates of efficacy. It has been suggested that this might be due to either sham protocols not being truly inert, or shortcomings in the design and execution of verum protocols, such as inappropriate frequency and duration of acupuncture treatment, or inappropriate electrical frequency in EA protocols.[17,18,63,68,69] Although these issues have been debated for decades, many SRs do not account for negative bias which may occur in conclusions due to potential underestimation of effect sizes.[70] Whenever the comparator is standard care, waitlist, or no treatment, the verum intervention shows large differences from the comparator. However, when a sham control is used, the differences are much smaller. This problem does not appear to be limited to acupuncture alone, but can also be seen in research into other complex interventions involving a skilled practitioner, such as psychiatry and surgery.[71,72] The task of separating specific and non-specific effects (which may include expectation effects) in complex medical interventions remains problematic.

In the development of clinical practice guidelines, an overreliance on efficacy measures alone without due consideration of effectiveness compared to other interventions, including standard care, risks underutilisation of acupuncture in healthcare systems. Tools to measure comparative effectiveness between various interventions, such as network meta-analyses, may be useful to include in considerations when developing clinical practice guidelines.

Mechanisms of acupuncture and EA analgesia are complex and differ between inflammatory, neuropathic, and visceral pain conditions. Research into neural pathways, mediators and their respective receptors, and signalling pathways is ongoing. Some common themes appear to be emerging. Acupuncture and EA appear to produce neuromodulation of central and peripheral nervous systems, resulting in lasting relief in chronic pain. Adverse neuroplasticity in the somatosensory cortex has been shown to be reversed by EA which may have potential applications in chronic complex pain conditions involving pathological neuroplasticity. Acupuncture may also relieve chronic pain by enhancement of glymphatic drainage, reducing norepinephrine and improving sleep quality. Reducing norepinephrine may also contribute to preventing acute pain from becoming chronic.

Conclusions

Despite the negative bias which may occur due to the potential underestimation of effect sizes of acupuncture and EA in studies, there remains high and moderate certainty evidence of acupuncture's effectiveness in the relief of numerous types of acute and chronic pain, and studies consistently report low risk profiles. Furthermore, acupuncture has been shown to be able to reverse adverse neuroplasticity in the somatosensory cortex and appears to produce lasting modulation in the central and peripheral nervous systems leading to long-term pain relief. This is further supported by an increasing understanding of the analgesic, antihyperalgesic, and anti-inflammatory effects of acupuncture and EA. A greater utilisation of acupuncture and EA for pain relief in healthcare settings has the potential to reduce reliance on less satisfactory options for pain management such as opioid medications.[70]

Further research is needed to explore aspects of acupuncture treatment for pain including optimal acupuncture point selection, appropriate frequency and duration of treatment, as well as optimal stimulation frequencies for EA. The relative merits of manual acupuncture vs EA in managing different types of pain also need to be clarified. Future studies may also improve understanding of how modulation of short-lived mediators such as endogenous opioids, serotonin, and adenosine can contribute to lasting neuromodulation. While some forms of acupuncture analgesia can be explained in terms of production and release of mediators such as endogenous opioids, acupuncture sometimes produces immediate pain relief which is too rapid for endogenous opioids. This question could also be a suitable target for further research.

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